

IN THE CLAIMS:

Please cancel claims 21-27 without prejudice to future presentation.

Please add new claims 28-36.

1-27. Canceled

28. (New) A method for identifying new proteasome inhibitors comprising:

obtaining eukaryotic cells;

lysing the cells, thereby producing a crude extract;

removing insoluble components from the crude extract, thereby producing a refined extract;

separating the refined extract into a first set of fractions by chromatographic separation via an ion exchange medium;

testing the first set of fractions for proteolytic activity;

isolating at least one proteolytically active fraction from the first set of fractions;

combining the isolated at least one proteolytically active fraction with any other proteolytically active fractions of the first set of fractions into a first pooled sample;

separating the first pooled sample into a second set of fractions by chromatographic separation over hydroxyapatite;

testing the second set of fractions for proteolytic activity;

isolating at least one proteolytically active fraction from the second set of fractions;

combining the isolated at least one proteolytically active fraction with any other proteolytically active fractions of the second set of fractions into a second pooled sample;

concentrating the second pooled sample into a concentrate;

separating the concentrate into a third set of fractions by chromatographic separation over a gel filtration medium;

testing the third set of fractions for proteolytic activity;

isolating at least one proteolytically active fraction from the third set of fractions;

combining the isolated at least one proteolytically active fraction with any other proteolytically active fractions of the third set of fractions into a third pooled sample;

crystallizing the third pooled sample;

analyzing the structure of the resulting crystals to identify new proteasome inhibitors.

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29. (New) The method of claim 28, wherein analyzing the structure of the resulting crystals comprises obtaining crystal structure data of the resulting crystals.

30. (New) The method of claim 29, wherein the crystal structure data is from the region of the proteasome pockets S1 of the subunits $\beta 1$ /PRE2, $\beta 2$ /PUP2 and $\beta 5$ /PRE2.

31. (New) The method of claim 28, wherein analyzing the structure of the resulting crystals comprises processing crystal structure data with a computer-aided modeling program.

32. (New) The method of claim 31, wherein the computer-aided modeling program modifies

crystal structure data of a yeast proteasome with amino acid sequences from the human proteasome.

33. (New) The method of claim 28, wherein the proteasome inhibitors have a three-dimensional structure that is complementary to proteasome pockets S1 of the subunits $\beta 1$ /PRE2, $\beta 2$ /PUP2 and $\beta 5$ /PRE2.

34. (New) The method of claim 28, wherein the testing of the first, second, and third sets of fractions each comprise two determinations of the proteolytic activity, one carried out in the absence of and the other in the presence of a proteasome inhibitor.

35. (New) The method of claim 28, wherein the resulting crystals contain a proteasome inhibitor.

36. (New) A proteasome inhibitor identified by the method of claim 28.
